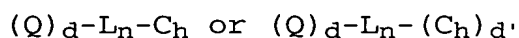


**WHAT IS CLAIMED IS:**

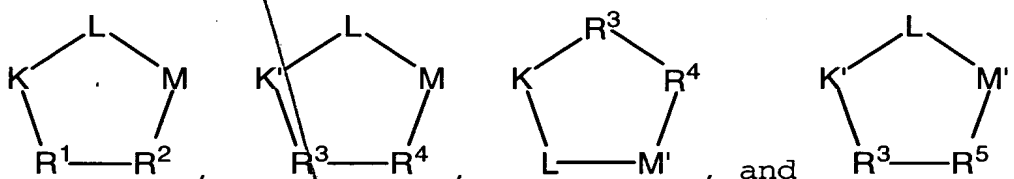
1. A compound, comprising: a targeting moiety and a chelator, wherein the targeting moiety is bound to the chelator, is a peptide or peptidomimetic, and binds to a receptor that is upregulated during angiogenesis and the compound has 0-1 linking groups between the targeting moiety and chelator.

2. A compound according to Claim 1, wherein the targeting moiety is a peptide or a mimetic thereof and the receptor is selected from the group: EGFR, FGFR, PDGFR, Flk-1/KDR, Flt-1, Tek, Tie, neuropilin-1, endoglin, endosialin, Axl,  $\alpha_v\beta_3$ ,  $\alpha_v\beta_5$ ,  $\alpha_5\beta_1$ ,  $\alpha_4\beta_1$ ,  $\alpha_1\beta_1$ , and  $\alpha_2\beta_2$  and the linking group is present between the targeting moiety and chelator.

3. A compound according to Claim 2, the receptor is the integrin  $\alpha_v\beta_3$  and the compound is of the formula:



wherein, Q is a peptide independently selected from the group:



K is an L-amino acid independently selected at each occurrence from the group: arginine, citrulline, N-methylarginine, lysine, homolysine, 2-aminoethylcysteine,  $\delta$ -N-2-imidazolinylnornithine,  $\delta$ -N-benzylcarbamoylnornithine, and  $\beta$ -2-benzimidazolylacetyl-1,2-diaminopropionic acid;

K' is a D-amino acid independently selected at each occurrence from the group: arginine, citrulline, N-methylarginine, lysine, homolysine, 2-aminoethylcysteine,

$\delta$ -N-2-imidazolinylnornithine,  
 $\delta$ -N-benzylcarbamoylnornithine, and  
 $\beta$ -2-benzimidazolylacetyl-1,2-diaminopropionic acid;

5 L is independently selected at each occurrence from the group:  
glycine, L-alanine, and D-alanine;

M is L-aspartic acid;

10 M' is D-aspartic acid;

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BI  
cont  
15 R<sup>1</sup> is an amino acid substituted with 0-1 bonds to L<sub>n</sub>,  
independently selected at each occurrence from the group:  
glycine, L-valine, D-valine, alanine, leucine,  
isoleucine, norleucine, 2-aminobutyric acid,  
2-aminohexanoic acid, tyrosine, phenylalanine,  
thienylalanine, phenylglycine, cyclohexylalanine,  
homophenylalanine, 1-naphthylalanine, lysine, serine,  
20 ornithine, 1,2-diaminobutyric acid, 1,2-diaminopropionic  
acid, cysteine, penicillamine, and methionine;

25 R<sup>2</sup> is an amino acid, substituted with 0-1 bonds to L<sub>n</sub>,  
independently selected at each occurrence from the group:  
glycine, valine, alanine, leucine, isoleucine,  
norleucine, 2-aminobutyric acid, 2-aminohexanoic acid,  
tyrosine, L-phenylalanine, D-phenylalanine,  
thienylalanine, phenylglycine, biphenylglycine,  
cyclohexylalanine, homophenylalanine,  
L-1-naphthylalanine, D-1-naphthylalanine, lysine, serine,  
30 ornithine, 1,2-diaminobutyric acid, 1,2-diaminopropionic  
acid, cysteine, penicillamine, methionine, and  
2-aminothiazole-4-acetic acid;

35 R<sup>3</sup> is an amino acid, substituted with 0-1 bonds to L<sub>n</sub>,  
independently selected at each occurrence from the group:  
glycine, D-valine, D-alanine, D-leucine, D-isoleucine,  
D-norleucine, D-2-aminobutyric acid, D-2-aminohexanoic  
acid, D-tyrosine, D-phenylalanine, D-thienylalanine,

D-phenylglycine, D-cyclohexylalanine,  
D-homophenylalanine, D-1-naphthylalanine, D-lysine,  
D-serine, D-ornithine, D-1,2-diaminobutyric acid,  
D-1,2-diaminopropionic acid, D-cysteine, D-penicillamine,  
and D-methionine;

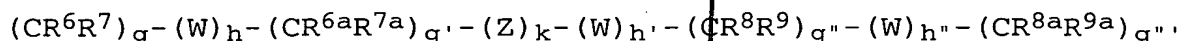
$R^4$  is an amino acid, substituted with 0-1 bonds to  $L_n$ , independently selected at each occurrence from the group: glycine, D-valine, D-alanine, D-leucine, D-isoleucine, D-norleucine, D-2-aminobutyric acid, D-2-aminohexanoic acid, D-tyrosine, D-phenylalanine, D-thienylalanine, D-phenylglycine, D-cyclohexylalanine, D-homophenylalanine, D-1-naphthylalanine, D-lysine, D-serine, D-ornithine, D-1,2-diaminobutyric acid, D-1,2-diaminopropionic acid, D-cysteine, D-penicillamine, D-methionine, and 2-aminothiazole-4-acetic acid;

R<sup>5</sup> is an amino acid, substituted with 0-1 bonds to L<sub>n</sub>, independently selected at each occurrence from the group: glycine, L-valine, L-alanine, L-leucine, L-isoleucine, L-norleucine, L-2-aminobutyric acid, L-2-aminohexanoic acid, L-tyrosine, L-phenylalanine, L-thienylalanine, L-phenylglycine, L-cyclohexylalanine, L-homophenylalanine, L-1-naphthylalanine, L-lysine, L-serine, L-ornithine, L-1,2-diaminobutyric acid, L-1,2-diaminopropionic acid, L-cysteine, L-penicillamine, L-methionine, and 2-aminothiazole-4-acetic acid;

provided that one of R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup>, R<sup>4</sup>, and R<sup>5</sup> in each Q is substituted with a bond to L<sub>n</sub>, further provided that when R<sup>2</sup> is 2-aminothiazole-4-acetic acid, K is N-methylarginine, further provided that when R<sup>4</sup> is 2-aminothiazole-4-acetic acid, K and K' are N-methylarginine, and still further provided that when R<sup>5</sup> is 2-aminothiazole-4-acetic acid, K' is N-methylarginine;

d is selected from /1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;

$L_n$  is a linking group having the formula:



5 provided that  $g+h+g'+k+h'+g''+h'''+g'''$  is other than 0;

W is independently selected at each occurrence from the group:

10 O, S, NH, NHC(=O), C(=O)NH, C(=O), C(=O)O, OC(=O),  
NHC(=S)NH, NHC(=O)NH, SO<sub>2</sub>, (OCH<sub>2</sub>CH<sub>2</sub>)<sub>s</sub>, (CH<sub>2</sub>CH<sub>2</sub>O)<sub>s'</sub>,  
(OCH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>)<sub>s''</sub>, (CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>O)<sub>t</sub>, and (aa)<sub>t'</sub>;

aa is independently at each occurrence an amino acid;

15 Z is selected from the group: aryl substituted with 0-3 R<sup>10</sup>,  
C<sub>3-10</sub> cycloalkyl substituted with 0-3 R<sup>10</sup>, and a 5-10  
membered heterocyclic ring system containing 1-4  
heteroatoms independently selected from N, S, and O and  
substituted with 0-3 R<sup>10</sup>;

20 R<sup>6</sup>, R<sup>6a</sup>, R<sup>7</sup>, R<sup>7a</sup>, R<sup>8</sup>, R<sup>8a</sup>, R<sup>9</sup> and R<sup>9a</sup> are independently selected  
at each occurrence from the group: H, =O, COOH, SO<sub>3</sub>H,  
PO<sub>3</sub>H, C<sub>1-5</sub> alkyl substituted with 0-3 R<sup>10</sup>, aryl  
substituted with 0-3 R<sup>10</sup>, benzyl substituted with 0-3  
R<sup>10</sup>, and C<sub>1-5</sub> alkoxy substituted with 0-3 R<sup>10</sup>,  
25 NHC(=O)R<sup>11</sup>, C(=O)NHR<sup>11</sup>, NHC(=O)NHR<sup>11</sup>, NHR<sup>11</sup>, R<sup>11</sup>, and a  
bond to C<sub>H</sub>;

30 R<sup>10</sup> is independently selected at each occurrence from the  
group: a bond to C<sub>H</sub>, COOR<sup>11</sup>, OH, NHR<sup>11</sup>, SO<sub>3</sub>H, PO<sub>3</sub>H, aryl  
substituted with 0-3 R<sup>11</sup>, C<sub>1-5</sub> alkyl substituted with 0-1  
R<sup>12</sup>, C<sub>1-5</sub> alkoxy substituted with 0-1 R<sup>12</sup>, and a 5-10  
membered heterocyclic ring system containing 1-4  
heteroatoms independently selected from N, S, and O and  
substituted with 0-3 R<sup>11</sup>;

35 R<sup>11</sup> is independently selected at each occurrence from the  
group: H, aryl substituted with 0-1 R<sup>12</sup>, a 5-10 membered  
heterocyclic ring system containing 1-4 heteroatoms

independently selected from N, S, and O and substituted with 0-1 R<sup>12</sup>, C<sub>3-10</sub> cycloalkyl substituted with 0-1 R<sup>12</sup>, polyalkylene glycol substituted with 0-1 R<sup>12</sup>, carbohydrate substituted with 0-1 R<sup>12</sup>, cyclodextrin substituted with 0-1 R<sup>12</sup>, amino acid substituted with 0-1 R<sup>12</sup>, polycarboxyalkyl substituted with 0-1 R<sup>12</sup>, polyazaalkyl substituted with 0-1 R<sup>12</sup>, peptide substituted with 0-1 R<sup>12</sup>, wherein the peptide is comprised of 2-10 amino acids, and a bond to C<sub>h</sub>;

R<sup>12</sup> is a bond to C<sub>h</sub>;

k is selected from 0, 1, and 2;

h is selected from 0, 1, and 2;

h' is selected from 0, 1, 2, 3, 4, and 5;

h'' is selected from 0, 1, 2, 3, 4, and 5;

g is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;

g' is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;

g'' is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;

g''' is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;

s is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;

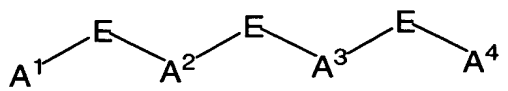
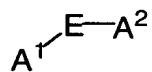
s' is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;

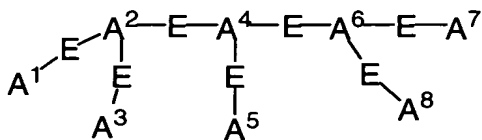
s'' is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;

t is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;

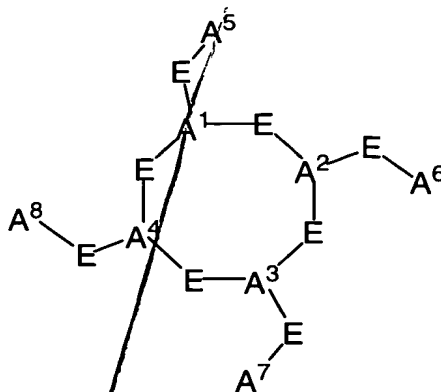
t' is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;

C<sub>h</sub> is a metal bonding unit having a formula selected from the group:





, and



A<sup>1</sup>, A<sup>2</sup>, A<sup>3</sup>, A<sup>4</sup>, A<sup>5</sup>, A<sup>6</sup>, A<sup>7</sup>, and A<sup>8</sup> are independently selected at each occurrence from the group N, NR<sup>13</sup>, NR<sup>13</sup>R<sup>14</sup>, S, SH, S(Pg), O, OH, PR<sup>13</sup>, PR<sup>13</sup>R<sup>14</sup>, P(O)R<sup>15</sup>R<sup>16</sup>, and a bond to L<sub>n</sub>;

E is a bond, CH, or a spacer group independently selected at each occurrence from the group: C<sub>1</sub>-C<sub>10</sub> alkyl substituted with 0-3 R<sup>17</sup>, aryl substituted with 0-3 R<sup>17</sup>, C<sub>3</sub>-<sub>10</sub> cycloalkyl substituted with 0-3 R<sup>17</sup>, heterocyclo-C<sub>1</sub>-<sub>10</sub> alkyl substituted with 0-3 R<sup>17</sup>, wherein the heterocyclo group is a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O, C<sub>6</sub>-<sub>10</sub> aryl-C<sub>1</sub>-<sub>10</sub> alkyl substituted with 0-3 R<sup>17</sup>, C<sub>1</sub>-<sub>10</sub> alkyl-C<sub>6</sub>-<sub>10</sub> aryl- substituted with 0-3 R<sup>17</sup>, and a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O and substituted with 0-3 R<sup>17</sup>;

R<sup>13</sup>, and R<sup>14</sup> are each independently selected from the group: a bond to L<sub>n</sub>, hydrogen, C<sub>1</sub>-C<sub>10</sub> alkyl substituted with 0-3 R<sup>17</sup>, aryl substituted with 0-3 R<sup>17</sup>, C<sub>1</sub>-<sub>10</sub> cycloalkyl substituted with 0-3 R<sup>17</sup>, heterocyclo-C<sub>1</sub>-<sub>10</sub> alkyl substituted with 0-3 R<sup>17</sup>, wherein the heterocyclo group is a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O, C<sub>6</sub>-<sub>10</sub> aryl-C<sub>1</sub>-<sub>10</sub> alkyl substituted with 0-3 R<sup>17</sup>, C<sub>1</sub>-<sub>10</sub> alkyl-C<sub>6</sub>-<sub>10</sub> aryl- substituted with 0-3 R<sup>17</sup>, a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O and

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substituted with 0-3 R<sup>17</sup>, and an electron, provided that when one of R<sup>13</sup> or R<sup>14</sup> is an electron, then the other is also an electron;

5 alternatively, R<sup>13</sup> and R<sup>14</sup> combine to form =C(R<sup>20</sup>)(R<sup>21</sup>);

15 R<sup>15</sup> and R<sup>16</sup> are each independently selected from the group: a bond to L<sub>n</sub>, -OH, C<sub>1</sub>-C<sub>10</sub> alkyl substituted with 0-3 R<sup>17</sup>, C<sub>1</sub>-C<sub>10</sub> alkyl substituted with 0-3 R<sup>17</sup>, aryl substituted with 0-3 R<sup>17</sup>, C<sub>3</sub>-<sub>10</sub> cycloalkyl substituted with 0-3 R<sup>17</sup>, heterocyclo-C<sub>1</sub>-<sub>10</sub> alkyl substituted with 0-3 R<sup>17</sup>, wherein the heterocyclo group is a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O, C<sub>6</sub>-<sub>10</sub> aryl-C<sub>1</sub>-<sub>10</sub> alkyl substituted with 0-3 R<sup>17</sup>, C<sub>1</sub>-<sub>10</sub> alkyl-C<sub>6</sub>-<sub>10</sub> aryl-substituted with 0-3 R<sup>17</sup>, and a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O and substituted with 0-3 R<sup>17</sup>;

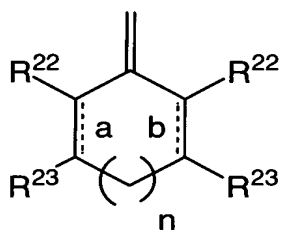
20 R<sup>17</sup> is independently selected at each occurrence from the group: a bond to L<sub>n</sub>, =O, F, Cl, Br, I, -CF<sub>3</sub>, -CN, -CO<sub>2</sub>R<sup>18</sup>, -C(=O)R<sup>18</sup>, -C(=O)N(R<sup>18</sup>)<sub>2</sub>, -CHO, -CH<sub>2</sub>OR<sup>18</sup>, -OC(=O)R<sup>18</sup>, -OC(=O)OR<sup>18a</sup>, -OR<sup>18</sup>, -OC(=O)N(R<sup>18</sup>)<sub>2</sub>, -NR<sup>19</sup>C(=O)R<sup>18</sup>, -NR<sup>19</sup>C(=O)OR<sup>18a</sup>, -NR<sup>19</sup>C(=O)N(R<sup>18</sup>)<sub>2</sub>, -NR<sup>19</sup>SO<sub>2</sub>N(R<sup>18</sup>)<sub>2</sub>, -NR<sup>19</sup>SO<sub>2</sub>R<sup>18a</sup>, -SO<sub>3</sub>H, -SO<sub>2</sub>R<sup>18a</sup>, -SR<sup>18</sup>, -S(=O)R<sup>18a</sup>, -SO<sub>2</sub>N(R<sup>18</sup>)<sub>2</sub>, -N(R<sup>18</sup>)<sub>2</sub>, -NHC(=S)NHR<sup>18</sup>, =NOR<sup>18</sup>, NO<sub>2</sub>, -C(=O)NHR<sup>18</sup>, -C(=O)NHN(R<sup>18</sup>)<sub>2</sub>, -OCH<sub>2</sub>CO<sub>2</sub>H, 2-(1-morpholino)ethoxy, C<sub>1</sub>-C<sub>5</sub> alkyl, C<sub>2</sub>-C<sub>4</sub> alkenyl, C<sub>3</sub>-C<sub>6</sub> cycloalkyl, C<sub>3</sub>-C<sub>6</sub> cycloalkylmethyl, C<sub>2</sub>-C<sub>6</sub> alkoxyalkyl, aryl substituted with 0-2 R<sup>18</sup>, and a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O;

35 R<sup>18</sup>, R<sup>18a</sup>, and R<sup>19</sup> are independently selected at each occurrence from the group: a bond to L<sub>n</sub>, H, C<sub>1</sub>-C<sub>6</sub> alkyl, phenyl, benzyl, C<sub>1</sub>-C<sub>6</sub> alkoxy, halide, nitro, cyano, and trifluoromethyl;

Pg is a thiol protecting group;

5  $R^{20}$  and  $R^{21}$  are independently selected from the group: H,  
C<sub>1</sub>-C<sub>10</sub> alkyl, -CN, -CO<sub>2</sub>R<sup>25</sup>, -C(=O)R<sup>25</sup>, -C(=O)N(R<sup>25</sup>)<sub>2</sub>,  
C<sub>2</sub>-C<sub>10</sub> 1-alkene substituted with 0-3 R<sup>23</sup>, C<sub>2</sub>-C<sub>10</sub> 1-alkyne  
substituted with 0-3 R<sup>23</sup>, aryl substituted with 0-3 R<sup>23</sup>,  
unsaturated 5-10 membered heterocyclic ring system  
10 containing 1-4 heteroatoms independently selected from N,  
S, and O and substituted with 0-3 R<sup>23</sup>, and unsaturated  
C<sub>3</sub>-10 carbocycle substituted with 0-3 R<sup>23</sup>;

alternatively,  $R^{20}$  and  $R^{21}$ , taken together with the divalent  
carbon radical to which they are attached form:



20  $R^{22}$  and  $R^{23}$  are independently selected from the group: H,  $R^{24}$ ,  
C<sub>1</sub>-C<sub>10</sub> alkyl substituted with 0-3  $R^{24}$ , C<sub>2</sub>-C<sub>10</sub> alkenyl  
substituted with 0-3  $R^{24}$ , C<sub>2</sub>-C<sub>10</sub> alkynyl substituted with  
0-3  $R^{24}$ , aryl substituted with 0-3  $R^{24}$ , a 5-10 membered  
heterocyclic ring system containing 1-4 heteroatoms  
independently selected from N, S, and O and substituted  
with 0-3  $R^{24}$ , and C<sub>3</sub>-10 carbocycle substituted with 0-3  
 $R^{24}$ ;

25 alternatively,  $R^{22}$ ,  $R^{23}$  taken together form a fused aromatic  
or a 5-10 membered heterocyclic ring system containing  
1-4 heteroatoms independently selected from N, S, and O;

30 **a** and **b** indicate the positions of optional double bonds and **n**  
is 0 or 1;



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5 *Sub*  
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$R^{24}$  is independently selected at each occurrence from the group:  $=O$ ,  $F$ ,  $Cl$ ,  $Br$ ,  $I$ ,  $-CF_3$ ,  $-CN$ ,  $-CO_2R^{25}$ ,  $-C(=O)R^{25}$ ,  $-C(=O)N(R^{25})_2$ ,  $-N(R^{25})_3^+$ ,  $-CH_2OR^{25}$ ,  $-OC(=O)R^{25}$ ,  $-OC(=O)OR^{25a}$ ,  $-OR^{25}$ ,  $-OC(=O)N(R^{25})_2$ ,  $-NR^{26}C(=O)R^{25}$ ,  $-NR^{26}C(=O)OR^{25a}$ ,  $-NR^{26}C(=O)N(R^{25})_2$ ,  $-NR^{26}SO_2N(R^{25})_2$ ,  $-NR^{26}SO_2R^{25a}$ ,  $-SO_3H$ ,  $-SO_2R^{25a}$ ,  $-SR^{25}$ ,  $-S(=O)R^{25a}$ ,  $-SO_2N(R^{25})_2$ ,  $-N(R^{25})_2$ ,  $=NOR^{25}$ ,  $-C(=O)NHOR^{25}$ ,  $-OCH_2CO_2H$ , and 2-(1-morpholino)ethoxy; and,

10  $R^{25}$ ,  $R^{25a}$ , and  $R^{26}$  are each independently selected at each occurrence from the group: hydrogen and  $C_1$ - $C_6$  alkyl;

and a pharmaceutically acceptable salt thereof.

15 4. A compound according to Claim 3, the present invention provides a compound, wherein:

20 L is glycine;

25  $R^1$  is an amino acid, optionally substituted with a bond to  $L_n$ , independently selected at each occurrence from the group: L-valine, D-valine, alanine, leucine, isoleucine, norleucine, 2-aminobutyric acid, tyrosine, phenylalanine, phenylglycine, cyclohexylalanine, homophenylalanine, lysine, ornithine, 1,2-diaminobutyric acid, and 1,2-diaminopropionic acid;

30  $R^2$  is an amino acid, optionally substituted with a bond to  $L_n$ , independently selected at each occurrence from the group: valine, alanine, leucine, isoleucine, norleucine, 2-aminobutyric acid, tyrosine, L-phenylalanine, D-phenylalanine, thienylalanine, phenylglycine, biphenylglycine, cyclohexylalanine, homophenylalanine, 35 L-1-naphthylalanine, D-1-naphthylalanine, lysine, ornithine, 1,2-diaminobutyric acid, 1,2-diaminopropionic acid, and 2-aminothiazole-4-acetic acid;

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R<sup>3</sup> is an amino acid, optionally substituted with a bond to L<sub>n</sub>, independently selected at each occurrence from the group: D-valine, D-alanine, D-leucine, D-isoleucine, D-norleucine, D-2-aminobutyric acid, D-tyrosine, D-phenylalanine, D-phenylglycine, D-cyclohexylalanine, D-homophenylalanine, D-lysine, D-serine, D-ornithine, D-1,2-diaminobutyric acid, and D-1,2-diaminopropionic acid;

R<sup>4</sup> is an amino acid, optionally substituted with a bond to L<sub>n</sub>, independently selected at each occurrence from the group: D-valine, D-alanine, D-leucine, D-isoleucine, D-norleucine, D-2-aminobutyric acid, D-tyrosine, D-phenylalanine, D-thienylalanine, D-phenylglycine, D-cyclohexylalanine, D-homophenylalanine, D-1-naphthylalanine, D-lysine, D-ornithine, D-1,2-diaminobutyric acid, D-1,2-diaminopropionic acid, and 2-aminothiazole-4-acetic acid;

R<sup>5</sup> is an amino acid, optionally substituted with a bond to L<sub>n</sub>, independently selected at each occurrence from the group: L-valine, L-alanine, L-leucine, L-isoleucine, L-norleucine, L-2-aminobutyric acid, L-tyrosine, L-phenylalanine, L-thienylalanine, L-phenylglycine, L-cyclohexylalanine, L-homophenylalanine, L-1-naphthylalanine, L-lysine, L-ornithine, L-1,2-diaminobutyric acid, L-1,2-diaminopropionic acid, and 2-aminothiazole-4-acetic acid;

d is selected from 1, 2, and 3;

W is independently selected at each occurrence from the group: O, NH, NHC(=O), C(=O)NH, C(=O), C(=O)O, OC(=O), NHC(=S)NH, NHC(=O)NH, SO<sub>2</sub>, (OCH<sub>2</sub>CH<sub>2</sub>)<sub>s</sub>, (CH<sub>2</sub>CH<sub>2</sub>O)<sub>s'</sub>, (OCH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>)<sub>s''</sub>, and (CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>O)<sub>t</sub>,

Z is selected from the group: aryl substituted with 0-1 R<sup>10</sup>, C<sub>3-10</sub> cycloalkyl substituted with 0-1 R<sup>10</sup>, and a 5-10

membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O and substituted with 0-1 R<sup>10</sup>;

5 R<sup>6</sup>, R<sup>6a</sup>, R<sup>7</sup>, R<sup>7a</sup>, R<sup>8</sup>, R<sup>8a</sup>, R<sup>9</sup>, and R<sup>9a</sup> are independently selected at each occurrence from the group: H, =O, COOH, SO<sub>3</sub>H, C<sub>1</sub>-C<sub>5</sub> alkyl substituted with 0-1 R<sup>10</sup>, aryl substituted with 0-1 R<sup>10</sup>, benzyl substituted with 0-1 R<sup>10</sup>, and C<sub>1</sub>-C<sub>5</sub> alkoxy substituted with 0-1 R<sup>10</sup>,  
10 NHC(=O)R<sup>11</sup>, C(=O)NHR<sup>11</sup>, NHC(=O)NHR<sup>11</sup>, NHR<sup>11</sup>, R<sup>11</sup>, and a bond to C<sub>h</sub>;

R<sup>10</sup> is independently selected at each occurrence from the group: COOR<sup>11</sup>, OH, NHR<sup>11</sup>, SO<sub>3</sub>H, aryl substituted with  
15 0-1 R<sup>11</sup>, a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O and substituted with 0-1 R<sup>11</sup>, C<sub>1</sub>-C<sub>5</sub> alkyl substituted with 0-1 R<sup>12</sup>, C<sub>1</sub>-C<sub>5</sub> alkoxy substituted with 0-1 R<sup>12</sup>, and a bond to C<sub>h</sub>;

20 R<sup>11</sup> is independently selected at each occurrence from the group: H, aryl substituted with 0-1 R<sup>12</sup>, a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O and substituted  
25 with 0-1 R<sup>12</sup>, polyalkylene glycol substituted with 0-1 R<sup>12</sup>, carbohydrate substituted with 0-1 R<sup>12</sup>, cyclodextrin substituted with 0-1 R<sup>12</sup>, amino acid substituted with 0-1 R<sup>12</sup>, and a bond to C<sub>h</sub>;

30 k is 0 or 1;  
h is 0 or 1;  
h' is 0 or 1;  
s is selected from 0, 1, 2, 3, 4, and 5;  
s' is selected from 0, 1, 2, 3, 4, and 5;  
35 s" is selected from 0, 1, 2, 3, 4, and 5;  
t is selected from 0, 1, 2, 3, 4, and 5;

A<sup>1</sup>, A<sup>2</sup>, A<sup>3</sup>, A<sup>4</sup>, A<sup>5</sup>, A<sup>6</sup>, A<sup>7</sup>, and A<sup>8</sup> are independently selected at each occurrence from the group: NR<sup>13</sup>, NR<sup>13</sup>R<sup>14</sup>, S, SH, S(Pg), OH, and a bond to L<sub>n</sub>;

5 E is a bond, CH, or a spacer group independently selected at each occurrence from the group: C<sub>1</sub>-C<sub>10</sub> alkyl substituted with 0-3 R<sup>17</sup>, aryl substituted with 0-3 R<sup>17</sup>, C<sub>3-10</sub> cycloalkyl substituted with 0-3 R<sup>17</sup>, and a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms  
10 independently selected from N, S, and O and substituted with 0-3 R<sup>17</sup>;

R<sup>13</sup>, and R<sup>14</sup> are each independently selected from the group:  
15 a bond to L<sub>n</sub>, hydrogen, C<sub>1</sub>-C<sub>10</sub> alkyl substituted with 0-3 R<sup>17</sup>, aryl substituted with 0-3 R<sup>17</sup>, a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O and substituted with 0-3 R<sup>17</sup>, and an electron, provided that when one of R<sup>13</sup> or R<sup>14</sup> is an electron, then the other is also an  
20 electron;

alternatively, R<sup>13</sup> and R<sup>14</sup> combine to form =C(R<sup>20</sup>)(R<sup>21</sup>);

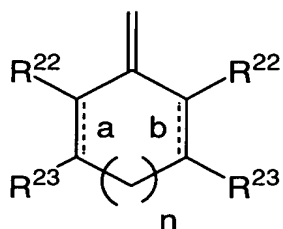
R<sup>17</sup> is independently selected at each occurrence from the  
25 group: a bond to L<sub>n</sub>, =O, F, Cl, Br, I, -CF<sub>3</sub>, -CN, -CO<sub>2</sub>R<sup>18</sup>, -C(=O)R<sup>18</sup>, -C(=O)N(R<sup>18</sup>)<sub>2</sub>, -CH<sub>2</sub>OR<sup>18</sup>, -OC(=O)R<sup>18</sup>, -OC(=O)OR<sup>18a</sup>, -OR<sup>18</sup>, -OC(=O)N(R<sup>18</sup>)<sub>2</sub>, -NR<sup>19</sup>C(=O)R<sup>18</sup>, -NR<sup>19</sup>C(=O)OR<sup>18a</sup>, -NR<sup>19</sup>C(=O)N(R<sup>18</sup>)<sub>2</sub>, -NR<sup>19</sup>SO<sub>2</sub>N(R<sup>18</sup>)<sub>2</sub>, -NR<sup>19</sup>SO<sub>2</sub>R<sup>18a</sup>, -SO<sub>3</sub>H, -SO<sub>2</sub>R<sup>18a</sup>, -S(=O)R<sup>18a</sup>, -SO<sub>2</sub>N(R<sup>18</sup>)<sub>2</sub>,  
30 -N(R<sup>18</sup>)<sub>2</sub>, -NHC(=S)NHR<sup>18</sup>, =NOR<sup>18</sup>, -C(=O)NHN(R<sup>18</sup>)R<sup>18a</sup>, -OCH<sub>2</sub>CO<sub>2</sub>H, and 2-(1-morpholino)ethoxy;

R<sup>18</sup>, R<sup>18a</sup>, and R<sup>19</sup> are independently selected at each  
occurrence from the group: a bond to L<sub>n</sub>, H, and C<sub>1</sub>-C<sub>6</sub>  
35 alkyl;

R<sup>20</sup> and R<sup>21</sup> are independently selected from the group: H, C<sub>1</sub>-C<sub>5</sub> alkyl, -CO<sub>2</sub>R<sup>25</sup>, C<sub>2</sub>-C<sub>5</sub> 1-alkene substituted with 0-3

R<sup>23</sup>, C<sub>2</sub>-C<sub>5</sub> 1-alkyne substituted with 0-3 R<sup>23</sup>, aryl substituted with 0-3 R<sup>23</sup>, and unsaturated 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O and substituted with 0-3 R<sup>23</sup>;

alternatively, R<sup>20</sup> and R<sup>21</sup>, taken together with the divalent carbon radical to which they are attached form:



R<sup>22</sup> and R<sup>23</sup> are independently selected from the group: H, and R<sup>24</sup>;

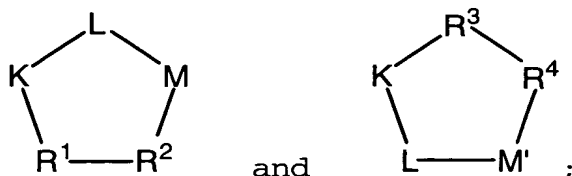
alternatively, R<sup>22</sup>, R<sup>23</sup> taken together form a fused aromatic or a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O;

R<sup>24</sup> is independently selected at each occurrence from the group: -CO<sub>2</sub>R<sup>25</sup>, -C(=O)N(R<sup>25</sup>)<sub>2</sub>, -CH<sub>2</sub>OR<sup>25</sup>, -OC(=O)R<sup>25</sup>, -OR<sup>25</sup>, -SO<sub>3</sub>H, -N(R<sup>25</sup>)<sub>2</sub>, and -OCH<sub>2</sub>CO<sub>2</sub>H; and,

R<sup>25</sup> is independently selected at each occurrence from the group: H and C<sub>1</sub>-C<sub>3</sub> alkyl.

5. A compound according to Claim 4, the present invention provides a compound, wherein:

Q is a peptide selected from the group:



$R^1$  is L-valine, D-valine, D-lysine optionally substituted on  
 the  $\epsilon$  amino group with a bond to  $L_n$  or L-lysine  
 5 optionally substituted on the  $\epsilon$  amino group with a bond  
 to  $L_n$ ;

$R^2$  is L-phenylalanine, D-phenylalanine, D-1-naphthylalanine,  
 2-aminothiazole-4-acetic acid, L-lysine optionally  
 10 substituted on the  $\epsilon$  amino group with a bond to  $L_n$  or  
 tyrosine, the tyrosine optionally substituted on the  
 hydroxy group with a bond to  $L_n$ ;

$R^3$  is D-valine, D-phenylalanine, or L-lysine optionally  
 15 substituted on the  $\epsilon$  amino group with a bond to  $L_n$ ;

$R^4$  is D-phenylalanine, D-tyrosine substituted on the hydroxy  
 group with a bond to  $L_n$ , or L-lysine optionally  
 20 substituted on the  $\epsilon$  amino group with a bond to  $L_n$ ;

provided that one of  $R^1$  and  $R^2$  in each  $Q$  is substituted with a  
 bond to  $L_n$ , and further provided that when  $R^2$  is  
 2-aminothiazole-4-acetic acid, K is N-methylarginine;

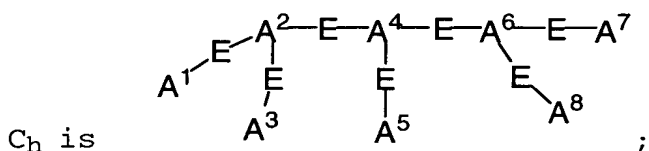
25 d is 1 or 2;

W is independently selected at each occurrence from the group:  
 $\text{NHC}(=\text{O})$ ,  $\text{C}(=\text{O})\text{NH}$ ,  $\text{C}(=\text{O})$ ,  $(\text{CH}_2\text{CH}_2\text{O})_s$ , and  $(\text{CH}_2\text{CH}_2\text{CH}_2\text{O})_t$ ;

30  $R^6$ ,  $R^{6a}$ ,  $R^7$ ,  $R^{7a}$ ,  $R^8$ ,  $R^{8a}$ ,  $R^9$ , and  $R^{9a}$  are independently  
 selected at each occurrence from the group: H,  
 $\text{NHC}(=\text{O})\text{R}^{11}$ , and a bond to  $\text{C}_h$ ;

k is 0;

$h''$  is selected from 0, 1, 2, and 3;  
 $g$  is selected from 0, 1, 2, 3, 4, and 5;  
 $g'$  is selected from 0, 1, 2, 3, 4, and 5;  
 $g''$  is selected from 0, 1, 2, 3, 4, and 5;  
5  $g'''$  is selected from 0, 1, 2, 3, 4, and 5;  
 $s'$  is 1 or 2;  
 $t$  is 1 or 2;



10  $A^1$  is selected from the group: OH, and a bond to  $L_n$ ;

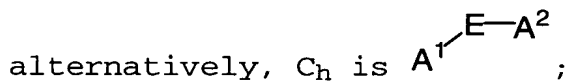
$A^2$ ,  $A^4$ , and  $A^6$  are each N;

15  $A^3$ ,  $A^5$ , and  $A^8$  are each OH;

$A^7$  is a bond to  $L_n$  or NH-bond to  $L_n$ ;

E is a  $C_2$  alkyl substituted with 0-1  $R^{17}$ ;

20  $R^{17}$  is =O;



25  $A^1$  is  $NH_2$  or  $N=C(R^{20})(R^{21})$ ;

E is a bond;

$A^2$  is  $NHR^{13}$ ;

30  $R^{13}$  is a heterocycle substituted with  $R^{17}$ , the heterocycle  
being selected from pyridine and pyrimidine;

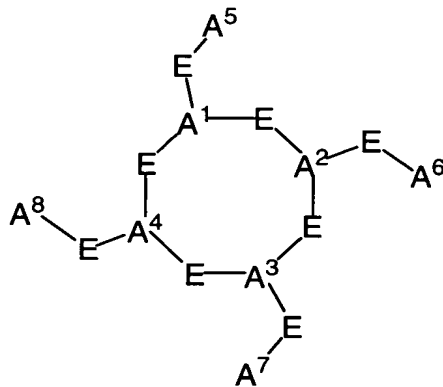
$R^{17}$  is selected from a bond to  $L_n$ ,  $C(=O)NHR^{18}$ , and  $C(=O)R^{18}$ ;

R<sup>18</sup> is a bond to L<sub>n</sub>;

R<sup>24</sup> is selected from the group: -CO<sub>2</sub>R<sup>25</sup>, -OR<sup>25</sup>, -SO<sub>3</sub>H, and -N(R<sup>25</sup>)<sub>2</sub>;

5

R<sup>25</sup> is independently selected at each occurrence from the group: hydrogen and methyl;



alternatively, C<sub>h</sub> is

10

A<sup>1</sup>, A<sup>2</sup>, A<sup>3</sup>, and A<sup>4</sup> are each N;

A<sup>5</sup>, A<sup>6</sup>, and A<sup>8</sup> are each OH;

15

A<sup>7</sup> is a bond to L<sub>n</sub>;

E is a C<sub>2</sub> alkyl substituted with 0-1 R<sup>17</sup>; and,

R<sup>17</sup> is =O.

20

6. A compound according to Claim 3, the present invention provides a compound selected from the group:

25

(a) cyclo{Arg-Gly-Asp-D-Tyr(N-[2-[[[5-[carbonyl]-2-pyridinyl]hydrazono]methyl]-benzenesulfonic acid]-3-aminopropyl)-Val};

30

(b) cyclo{Arg-Gly-Asp-D-Tyr((N-[2-[[[5-[carbonyl]-2-pyridinyl]hydrazono]methyl]-benzenesulfonic acid]-18-





- (1) {cyclo(Arg-D-Val-D-Tyr(N-[2-[[[5-[carbonyl]-2-pyridinyl]hydrazono]methyl]-benzenesulfonic acid]-3-aminopropyl)-D-Asp-Gly};
- 5 (m) cyclo{D-Lys([2-[[[5-[carbonyl]-2-pyridinyl]hydrazono]methyl]-benzenesulfonic acid])-D-Phe-D-Asp-Gly-Arg};
- 10 (n) [2-[[[5-[carbonyl]-2-pyridinyl]hydrazono]methyl]-benzenesulfonic acid]-Glu(cyclo{D-Lys-D-Phe-D-Asp-Gly-Arg})-cyclo{D-Lys-D-Phe-D-Asp-Gly-Arg};
- 15 (o) cyclo{D-Phe-D-Lys([2-[[[5-[carbonyl]-2-pyridinyl]hydrazono]methyl]-benzenesulfonic acid])-D-Asp-Gly-Arg};
- (p) cyclo{N-Me-Arg-Gly-Asp-ATA-D-Lys([2-[[[5-[carbonyl]-2-pyridinyl]hydrazono]methyl]-benzenesulfonic acid])};
- 20 (q) cyclo{Cit-Gly-Asp-D-Phe-Lys([2-[[[5-[carbonyl]-2-pyridinyl]hydrazono]methyl]-benzenesulfonic acid])};
- (r) 2-(1,4,7,10-tetraaza-4,7,10-tris(carboxymethyl)-1-cyclododecyl)acetyl-Glu(cyclo{Lys-Arg-Gly-Asp-D-Phe})-cyclo{Lys-Arg-Gly-Asp-D-Phe};
- 25 (s) cyclo{Arg-Gly-Asp-D-Phe-Lys(DTPA)};
- (t) cyclo{Arg-Gly-Asp-D-Phe-Lys}<sub>2</sub>(DTPA);
- 30 (u) Cyclo{Arg-Gly-Asp-D-Tyr(N-DTPA-3-aminopropyl)-Val};
- (v) cyclo{Orn(d-N-2-Imidazolinyl)-Gly-Asp-D-Tyr(N-[2-[[[5-[carbonyl]-2-pyridinyl]hydrazono]methyl]-benzenesulfonic acid]-3-aminopropyl)-Val};
- 35



(ff) cyclo{Orn(d-N-2-Imidazoliny1)-D-Val-D-Tyr(N-[2-[[[5-[carbonyl]-2-pyridiny1]hydrazono]methyl]-benzenesulfonic acid]-3-aminopropyl)-D-Asp-Gly};

5 or a pharmaceutically acceptable salt form thereof.

7. A kit comprising a compound of Claim 3, or a pharmaceutically acceptable salt form thereof and a  
10 pharmaceutically acceptable carrier.

8. A kit according to Claim 7, wherein the kit further comprises one or more ancillary ligands and a reducing agent.  
15

9. A kit according to Claim 8, wherein the ancillary ligands are tricine and TPPTS.  
20

10. A kit according to Claim 9, wherein the reducing agent is tin(II).  
25

11. A diagnostic or therapeutic metallopharmaceutical composition, comprising: a metal, a chelator capable of chelating the metal and a targeting moiety, wherein the targeting moiety is bound to the chelator, is a peptide or peptidomimetic and binds to a receptor that is upregulated during angiogenesis and the compound has 0-1 linking groups between the targeting moiety and chelator.  
30

12. A composition according to Claim 11, wherein the metallopharmaceutical is a diagnostic radiopharmaceutical, the metal is a radioisotope selected from the group: <sup>99m</sup>Tc, <sup>95</sup>Tc, <sup>111</sup>In, <sup>62</sup>Cu, <sup>64</sup>Cu, <sup>67</sup>Ga, and <sup>68</sup>Ga, the targeting moiety is a peptide or a mimetic thereof and the receptor is selected from  
35

the group: EGFR, FGFR, PDGFR, Flk-1/KDR, Flt-1, Tek, Tie, neuropilin-1, endoglin, endosialin, Axl,  $\alpha_v\beta_3$ ,  $\alpha_v\beta_5$ ,  $\alpha_5\beta_1$ ,  $\alpha_4\beta_1$ ,  $\alpha_1\beta_1$ , and  $\alpha_2\beta_2$  and the linking group is present between the targeting moiety and chelator.

13. A composition according to Claim 12, wherein the targeting moiety is a cyclic pentapeptide and the receptor is  $\alpha_v\beta_3$ .

14. A composition according to Claim 13, wherein the radioisotope is  $^{99m}\text{Tc}$  or  $^{95}\text{Tc}$ , the radiopharmaceutical further comprises a first ancillary ligand and a second ancillary ligand capable of stabilizing the radiopharmaceutical.

15. A composition according to Claim 14, wherein the radioisotope is  $^{99m}\text{Tc}$ .

16. A composition according to Claim 15, wherein the radiopharmaceutical is selected from the group:

- $^{99m}\text{Tc}(\text{tricine})(\text{TPPTS})(\text{cyclo}(\text{Arg-Gly-Asp-D-Tyr}(\text{N}-[[5-[\text{carbonyl}]-2\text{-pyridinyl}]\text{diazenido}]-3\text{-aminopropyl})-\text{Val}));$
- $^{99m}\text{Tc}(\text{tricine})(\text{TPPMS})(\text{cyclo}(\text{Arg-D-Val-D-Tyr}(\text{N}-[[5-[\text{carbonyl}]-2\text{-pyridinyl}]\text{diazenido}]-3\text{-aminopropyl})-\text{D-Asp-Gly}));$
- $^{99m}\text{Tc}(\text{tricine})(\text{TPPDS})(\text{cyclo}(\text{Arg-D-Val-D-Tyr}(\text{N}-[[5-[\text{carbonyl}]-2\text{-pyridinyl}]\text{diazenido}]-3\text{-aminopropyl})-\text{D-Asp-Gly}));$
- $^{99m}\text{Tc}(\text{tricine})(\text{TPPTS})(\text{cyclo}(\text{Arg-D-Val-D-Tyr}(\text{N}-[[5-[\text{carbonyl}]-2\text{-pyridinyl}]\text{diazenido}]-3\text{-aminopropyl})-\text{D-Asp-Gly}));$
- $^{99m}\text{Tc}(\text{tricine})(\text{TPPTS})(\text{cyclo}(\text{Arg-Gly-Asp-D-Phe-Lys}(\text{N}-[[5-[\text{carbonyl}]-2\text{-pyridinyl}]\text{diazenido}]));$



Glu(cyclo{D-Lys-D-Phe-D-Asp-Gly-Arg})-cyclo{D-Lys-D-Phe-D-Asp-Gly-Arg});

5  $^{99m}\text{Tc}(\text{tricine})(\text{TPPTS})(\text{cyclo}\{\text{D-Phe-D-Lys}([2-[[[5-[\text{carbonyl}]-2-\text{pyridinyl}]\text{hydrazono}]\text{methyl}]-\text{benzenesulfonic acid}])-\text{D-Asp-Gly-Arg}\}));$

10  $^{99m}\text{Tc}(\text{tricine})(\text{TPPTS})(\text{cyclo}(\text{N-Me-Arg-Gly-Asp-ATA-D-Lys}(\text{N}-[[5-[\text{carbonyl}]-2-\text{pyridinyl}]\text{diazenido}])))$ ;

$^{99m}\text{Tc}(\text{tricine})(\text{TPPTS})(\text{cyclo}\{\text{Cit-Gly-Asp-D-Phe-Lys}([2-[[[5-[\text{carbonyl}]-2-\text{pyridinyl}]\text{hydrazono}]\text{methyl}]-\text{benzenesulfonic acid}])))$ ; and,

15  $^{99m}\text{Tc}(\text{tricine})(1,2,4\text{-triazole})(\text{cyclo}(\text{Arg-Gly-Asp-D-Tyr}(\text{N}-[[5-[\text{carbonyl}]-2-\text{pyridinyl}]\text{diazenido}]-3\text{-aminopropyl})-\text{Val}))$ .

20 17. A composition according to Claim 13, wherein the radioisotope is  $^{111}\text{In}$ .

25 18. A composition according to Claim 17, wherein the radiopharmaceutical is selected from the group:

(DOTA- $^{111}\text{In}$ )-Glu(cyclo{Lys-Arg-Gly-Asp-D-Phe})-cyclo{Lys-Arg-Gly-Asp-D-Phe};

cyclo(Arg-Gly-Asp-D-Phe-Lys(DTPA- $^{111}\text{In}$ )); and,

30 cyclo(Arg-Gly-Asp-D-Phe-Lys) $_2$ (DTPA- $^{111}\text{In}$ ).

35 19. A composition according to Claim 11, wherein the metallopharmaceutical is a therapeutic radiopharmaceutical, the metal is a radioisotope selected from the group:  $^{186}\text{Re}$ ,  $^{188}\text{Re}$ ,  $^{153}\text{Sm}$ ,  $^{166}\text{Ho}$ ,  $^{177}\text{Lu}$ ,  $^{149}\text{Pm}$ ,  $^{90}\text{Y}$ ,  $^{212}\text{Bi}$ ,  $^{103}\text{Pd}$ ,  $^{109}\text{Pd}$ ,  $^{159}\text{Gd}$ ,  $^{140}\text{La}$ ,  $^{198}\text{Au}$ ,  $^{199}\text{Au}$ ,  $^{169}\text{Yb}$ ,  $^{175}\text{Yb}$ ,  $^{165}\text{Dy}$ ,  $^{166}\text{Dy}$ ,  $^{67}\text{Cu}$ ,

105Rh, 111Ag, and 192Ir, the targeting moiety is a peptide or a mimetic thereof and the receptor is selected from the group: EGFR, FGFR, PDGFR, Flk-1/KDR, Flt-1, Tek, Tie, neuropilin-1, endoglin, endosialin, Axl,  $\alpha_v\beta_3$ ,  $\alpha_v\beta_5$ ,  $\alpha_5\beta_1$ ,  $\alpha_4\beta_1$ ,  $\alpha_1\beta_1$ , and  $\alpha_2\beta_2$  and the linking group is present between the targeting moiety and chelator.

20. A composition according to Claim 19, wherein the targeting moiety is a cyclic pentapeptide and the receptor is  $\alpha_v\beta_3$ .

21. A composition according to Claim 20, wherein the radioisotope is  $^{153}\text{Sm}$ .

22. A composition according to Claim 21, wherein the radiopharmaceutical is selected from the group:

cyclo(Arg-Gly-Asp-D-Phe-Lys(DTPA- $^{153}\text{Sm}$ ));

cyclo(Arg-Gly-Asp-D-Phe-Lys)<sub>2</sub>(DTPA- $^{153}\text{Sm}$ ); and,

cyclo(Arg-Gly-Asp-D-Tyr(N-DTPA( $^{153}\text{Sm}$ )-3-aminopropyl)-Val).

23. A composition according to Claim 20, wherein the radioisotope is  $^{177}\text{Lu}$ .

24. A composition according to Claim 23, wherein the radiopharmaceutical is selected from the group:

cyclo(Arg-Gly-Asp-D-Phe-Lys(DTPA- $^{177}\text{Lu}$ ));

(DOTA- $^{177}\text{Lu}$ )-Glu(cyclo{Lys-Arg-Gly-Asp-D-Phe})-cyclo{Lys-Arg-Gly-Asp-D-Phe};



cyclo(Arg-Gly-Asp-D-Phe-Lys)<sub>2</sub>(DTPA-<sup>177</sup>Lu); and,

cyclo(Arg-Gly-Asp-D-Tyr(N-DTPA(<sup>177</sup>Lu)-3-aminopropyl)-Val).

5

25. A composition according to Claim 20, wherein the radioisotope is <sup>90</sup>Y.

10

26. A composition according to Claim 25, wherein the radiopharmaceutical is:

(DOTA-<sup>90</sup>Y)-Glu(cyclo{Lys-Arg-Gly-Asp-D-Phe})-cyclo{Lys-Arg-Gly-Asp-D-Phe};

15

27. A composition according to Claim 11, wherein the metallopharmaceutical is a MRI contrast agent, the metal is a paramagnetic metal ion selected from the group: Gd(III), Dy(III), Fe(III), and Mn(II), the targeting moiety is a peptide or a mimetic thereof and the receptor is selected from the group: EGFR, FGFR, PDGFR, Flk-1/KDR, Flt-1, Tek, Tie, neuropilin-1, endoglin, endosialin, Axl,  $\alpha_v\beta_3$ ,  $\alpha_v\beta_5$ ,  $\alpha_5\beta_1$ ,  $\alpha_4\beta_1$ ,  $\alpha_1\beta_1$ , and  $\alpha_2\beta_2$  and the linking group is present between the targeting moiety and chelator.

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28. A composition according to Claim 27, wherein the targeting moiety is a cyclic pentapeptide and the receptor is  $\alpha_v\beta_3$ .

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29. A composition according to Claim 28, wherein the metal ion is Gd(III).

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30. A composition according to Claim 29, wherein the contrast agent is:

cyclo(Arg-Gly-Asp-D-Tyr(N-DTPA(Gd(III))-3-aminopropyl)-Val).

5

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31. A composition according to Claim 11, wherein the metallopharmaceutical is a X-ray contrast agent, the metal is selected from the group: Re, Sm, Ho, Lu, Pm, Y, Bi, Pd, Gd, La, Au, Au, Yb, Dy, Cu, Rh, Ag, and Ir, the targeting moiety is a cyclic pentapeptide, the receptor is  $\alpha_v\beta_3$ , and the linking group is present between the targeting moiety and chelator.

15

32. A method of treating rheumatoid arthritis in a patient comprising: administering a therapeutic radiopharmaceutical of Claim 11 capable of localizing in new angiogenic vasculature to a patient by injection or infusion.

20

33. A method of treating cancer in a patient comprising: administering to a patient in need thereof a therapeutic radiopharmaceutical of Claim 11 by injection or infusion.

25

34. A method of imaging formation of new blood vessels in a patient comprising: (1) administering a diagnostic radiopharmaceutical, a MRI contrast agent, or a X-ray contrast agent of of Claim 11 to a patient by injection or infusion; (2) imaging the area of the patient wherein the desired formation of new blood vessels is located.

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35. A method of imaging cancer in a patient comprising: (1) administering a diagnostic radiopharmaceutical of Claim 12 to a patient by injection or infusion; (2) imaging the patient

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K is an L-amino acid independently selected at each occurrence from the group: arginine, citrulline, N-methylarginine, lysine, homolysine, 2-aminoethylcysteine,  $\delta$ -N-2-imidazolinylnornithine,  $\delta$ -N-benzylcarbamoylnornithine, and  $\beta$ -2-benzimidazolylacetyl-1,2-diaminopropionic acid;

K' is a D-amino acid independently selected at each occurrence from the group: arginine, citrulline, N-methylarginine, lysine, homolysine, 2-aminoethylcysteine,  $\delta$ -N-2-imidazolinylnornithine,  $\delta$ -N-benzylcarbamoylnornithine, and  $\beta$ -2-benzimidazolylacetyl-1,2-diaminopropionic acid;

L is independently selected at each occurrence from the group: glycine, L-alanine, and D-alanine;

M is L-aspartic acid;

M' is D-aspartic acid;

R<sup>1</sup> is an amino acid substituted with 0-1 bonds to L<sub>n</sub>, independently selected at each occurrence from the group: glycine, L-valine, D-valine, alanine, leucine, isoleucine, norleucine, 2-aminobutyric acid, 2-aminohexanoic acid, tyrosine, phenylalanine, thienylalanine, phenylglycine, cyclohexylalanine, homophenylalanine, 1-naphthylalanine, lysine, serine, ornithine, 1,2-diaminobutyric acid, 1,2-diaminopropionic acid, cysteine, penicillamine, and methionine;



acid, L-tyrosine, L-phenylalanine, L-thienylalanine,  
L-phenylglycine, L-cyclohexylalanine,  
L-homophenylalanine, L-1-naphthylalanine, L-lysine,  
L-serine, L-ornithine, L-1,2-diaminobutyric acid,  
5 L-1,2-diaminopropionic acid, L-cysteine, L-penicillamine,  
L-methionine, and 2-aminothiazole-4-acetic acid;

provided that one of  $R^1$ ,  $R^2$ ,  $R^3$ ,  $R^4$ , and  $R^5$  in each Q is  
substituted with a bond to  $L_n$ , further provided that when  
10  $R^2$  is 2-aminothiazole-4-acetic acid, K is  
N-methylarginine, further provided that when  $R^4$  is  
2-aminothiazole-4-acetic acid, K and K' are  
N-methylarginine, and still further provided that when  $R^5$   
is 2-aminothiazole-4-acetic acid, K' is N-methylarginine;

15 d is selected from 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;

$S_f$  is a surfactant which is a lipid or a compound of the

formula:  $A^9 - E^1 - A^{10}$  ;

20  $A^9$  is selected from the group: OH and  $OR^{27}$ ;

$A^{10}$  is  $OR^{27}$ ;

25  $R^{27}$  is  $C(=O)C_{1-20}$  alkyl;

$E^1$  is  $C_{1-10}$  alkylene substituted with 1-3  $R^{28}$ ;

30  $R^{28}$  is independently selected at each occurrence from the  
group:  $R^{30}$ ,  $-PO_3H-R^{30}$ ,  $=O$ ,  $-CO_2R^{29}$ ,  $-C(=O)R^{29}$ ,  
 $-C(=O)N(R^{29})_2$ ,  $-CH_2OR^{29}$ ,  $-OR^{29}$ ,  $-N(R^{29})_2$ ,  $C_1-C_5$  alkyl,  
and  $C_2-C_4$  alkenyl;

35  $R^{29}$  is independently selected at each occurrence from the  
group:  $R^{30}$ , H,  $C_1-C_6$  alkyl, phenyl, benzyl, and  
trifluoromethyl;

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$R^{30}$  is a bond to  $L_n$ ;

$L_n$  is a linking group having the formula:

5  $(CR^6R^7)_g-(W)_h-(CR^{6a}R^{7a})_{g'}-(Z)_k-(W)_{h'}-(CR^8R^9)_{g''}-(W)_{h''}-(CR^{8a}R^{9a})_{g'''}$ .

W is independently selected at each occurrence from the group:

O, S, NH, NHC(=O), C(=O)NH, C(=O), C(=O)O, OC(=O),  
NHC(=S)NH, NHC(=O)NH, SO<sub>2</sub>, (OCH<sub>2</sub>CH<sub>2</sub>)<sub>20-200</sub>, (CH<sub>2</sub>CH<sub>2</sub>O)<sub>20-</sub>  
10 200, (OCH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>)<sub>20-200</sub>, (CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>O)<sub>20-200</sub>, and (aa)<sub>t</sub>;

aa is independently at each occurrence an amino acid;

15 Z is selected from the group: aryl substituted with 0-3  $R^{10}$ ,  
C<sub>3-10</sub> cycloalkyl substituted with 0-3  $R^{10}$ , and a 5-10  
membered heterocyclic ring system containing 1-4  
heteroatoms independently selected from N, S, and O and  
substituted with 0-3  $R^{10}$ ;

20  $R^6$ ,  $R^{6a}$ ,  $R^7$ ,  $R^{7a}$ ,  $R^8$ ,  $R^{8a}$ ,  $R^9$  and  $R^{9a}$  are independently selected  
at each occurrence from the group: H, =O, COOH, SO<sub>3</sub>H,  
PO<sub>3</sub>H, C<sub>1-5</sub> alkyl substituted with 0-3  $R^{10}$ , aryl  
substituted with 0-3  $R^{10}$ , benzyl substituted with 0-3  
 $R^{10}$ , and C<sub>1-5</sub> alkoxy substituted with 0-3  $R^{10}$ ,  
25 NHC(=O) $R^{11}$ , C(=O)NHR<sup>11</sup>, NHC(=O)NHR<sup>11</sup>, NHR<sup>11</sup>,  $R^{11}$ , and a  
bond to  $S_f$ ;

$R^{10}$  is independently selected at each occurrence from the  
group: a bond to  $S_f$ , COOR<sup>11</sup>, OH, NHR<sup>11</sup>, SO<sub>3</sub>H, PO<sub>3</sub>H, aryl  
30 substituted with 0-3  $R^{11}$ , C<sub>1-5</sub> alkyl substituted with 0-1  
 $R^{12}$ , C<sub>1-5</sub> alkoxy substituted with 0-1  $R^{12}$ , and a 5-10  
membered heterocyclic ring system containing 1-4  
heteroatoms independently selected from N, S, and O and  
substituted with 0-3  $R^{11}$ ;

35  $R^{11}$  is independently selected at each occurrence from the  
group: H, aryl substituted with 0-1  $R^{12}$ , a 5-10 membered  
heterocyclic ring system containing 1-4 heteroatoms

independently selected from N, S, and O and substituted with 0-1 R<sup>12</sup>, C<sub>3-10</sub> cycloalkyl substituted with 0-1 R<sup>12</sup>, amino acid substituted with 0-1 R<sup>12</sup>, and a bond to S<sub>f</sub>;

5 R<sup>12</sup> is a bond to S<sub>f</sub>;

k is selected from 0, 1, and 2;

h is selected from 0, 1, and 2;

h' is selected from 0, 1, 2, 3, 4, and 5;

10 h'' is selected from 0, 1, 2, 3, 4, and 5;

g is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;

g' is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;

g'' is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;

g''' is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;

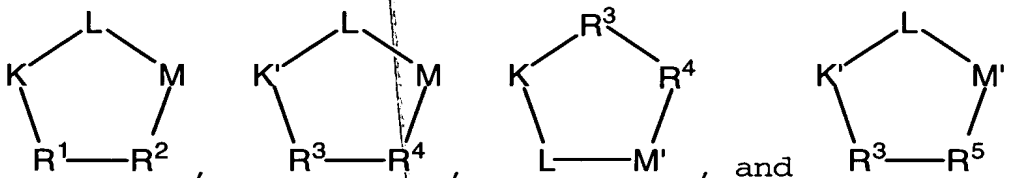
15 t' is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;

and a pharmaceutically acceptable salt thereof.

20 41. A compound according to Claim 40, wherein the compound is of the formula:



wherein, Q is a cyclic pentapeptide independently selected from the group:



30 K is an L-amino acid independently selected at each occurrence from the group: arginine, citrulline, N-methylarginine, lysine, homolysine, 2-aminoethylcysteine,  $\delta$ -N-2-imidazolinylnornithine,  $\delta$ -N-benzylcarbamoylnornithine, and  $\beta$ -2-benzimidazolylacetyl-1,2-diaminopropionic acid;



K' is a D-amino acid independently selected at each occurrence from the group: arginine, citrulline, N-methylarginine, lysine, homolysine, 2-aminoethylcysteine,  $\delta$ -N-2-imidazolinylnornithine,  $\delta$ -N-benzylcarbamoylnornithine, and  $\beta$ -2-benzimidazolylacetyl-1,2-diaminopropionic acid;

L is independently selected at each occurrence from the group: glycine, L-alanine, and D-alanine;

M is L-aspartic acid;

M' is D-aspartic acid;

R<sup>1</sup> is an amino acid substituted with 0-1 bonds to L<sub>n</sub>, independently selected at each occurrence from the group: glycine, L-valine, D-valine, alanine, leucine, isoleucine, norleucine, 2-aminobutyric acid, 2-aminohexanoic acid, tyrosine, phenylalanine, thienylalanine, phenylglycine, cyclohexylalanine, homophenylalanine, 1-naphthylalanine, lysine, serine, ornithine, 1,2-diaminobutyric acid, 1,2-diaminopropionic acid, cysteine, penicillamine, and methionine;

R<sup>2</sup> is an amino acid, substituted with 0-1 bonds to L<sub>n</sub>, independently selected at each occurrence from the group: glycine, valine, alanine, leucine, isoleucine, norleucine, 2-aminobutyric acid, 2-aminohexanoic acid, tyrosine, L-phenylalanine, D-phenylalanine, thienylalanine, phenylglycine, biphenylglycine, cyclohexylalanine, homophenylalanine, L-1-naphthylalanine, D-1-naphthylalanine, lysine, serine, ornithine, 1,2-diaminobutyric acid, 1,2-diaminopropionic acid, cysteine, penicillamine, methionine, and 2-aminothiazole-4-acetic acid;

R<sup>3</sup> is an amino acid, substituted with 0-1 bonds to L<sub>n</sub>, independently selected at each occurrence from the group:

glycine, D-valine, D-alanine, D-leucine, D-isoleucine,  
D-norleucine, D-2-aminobutyric acid, D-2-aminohexanoic  
acid, D-tyrosine, D-phenylalanine, D-thienylalanine,  
D-phenylglycine, D-cyclohexylalanine,  
5 D-homophenylalanine, D-1-naphthylalanine, D-lysine,  
D-serine, D-ornithine, D-1,2-diaminobutyric acid,  
D-1,2-diaminopropionic acid, D-cysteine, D-penicillamine,  
and D-methionine;

10  $R^4$  is an amino acid, substituted with 0-1 bonds to  $L_n$ ,  
independently selected at each occurrence from the group:  
glycine, D-valine, D-alanine, D-leucine, D-isoleucine,  
D-norleucine, D-2-aminobutyric acid, D-2-aminohexanoic  
acid, D-tyrosine, D-phenylalanine, D-thienylalanine,  
15 D-phenylglycine, D-cyclohexylalanine,  
D-homophenylalanine, D-1-naphthylalanine, D-lysine,  
D-serine, D-ornithine, D-1,2-diaminobutyric acid,  
D-1,2-diaminopropionic acid, D-cysteine, D-penicillamine,  
D-methionine, and 2-aminothiazole-4-acetic acid;

20  $R^5$  is an amino acid, substituted with 0-1 bonds to  $L_n$ ,  
independently selected at each occurrence from the group:  
glycine, L-valine, L-alanine, L-leucine, L-isoleucine,  
L-norleucine, L-2-aminobutyric acid, L-2-aminohexanoic  
25 acid, L-tyrosine, L-phenylalanine, L-thienylalanine,  
L-phenylglycine, L-cyclohexylalanine,  
L-homophenylalanine, L-1-naphthylalanine, L-lysine,  
L-serine, L-ornithine, L-1,2-diaminobutyric acid,  
L-1,2-diaminopropionic acid, L-cysteine, L-penicillamine,  
30 L-methionine, and 2-aminothiazole-4-acetic acid;

provided that one of  $R^1$ ,  $R^2$ ,  $R^3$ ,  $R^4$ , and  $R^5$  in each Q is  
substituted with a bond to  $L_n$ , further provided that when  
 $R^2$  is 2-aminothiazole-4-acetic acid, K is  
35 N-methylarginine, further provided that when  $R^4$  is  
2-aminothiazole-4-acetic acid, K and K' are  
N-methylarginine, and still further provided that when  $R^5$   
is 2-aminothiazole-4-acetic acid, K' is N-methylarginine;



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R<sup>6</sup>, R<sup>6a</sup>, R<sup>7</sup>, R<sup>7a</sup>, R<sup>8</sup>, R<sup>8a</sup>, R<sup>9</sup> and R<sup>9a</sup> are independently selected at each occurrence from the group: H, =O, C<sub>1</sub>-C<sub>5</sub> alkyl substituted with 0-3 R<sup>10</sup>, and C<sub>1</sub>-C<sub>5</sub> alkoxy substituted with 0-3 R<sup>10</sup>, and a bond to S<sub>f</sub>;

R<sup>10</sup> is independently selected at each occurrence from the group: a bond to S<sub>f</sub>, COOR<sup>11</sup>, OH, NHR<sup>11</sup>, C<sub>1</sub>-5 alkyl substituted with 0-1 R<sup>12</sup>, and C<sub>1</sub>-5 alkoxy substituted with 0-1 R<sup>12</sup>;

R<sup>11</sup> is independently selected at each occurrence from the group: H, aryl substituted with 0-1 R<sup>12</sup>, C<sub>3</sub>-10 cycloalkyl substituted with 0-1 R<sup>12</sup>, amino acid substituted with 0-1 R<sup>12</sup>, and a bond to S<sub>f</sub>;

R<sup>12</sup> is a bond to S<sub>f</sub>;

k is selected from 0, 1, and 2;

h is selected from 0, 1, and 2;

h' is selected from 0, 1, 2, 3, 4, and 5;

h" is selected from 0, 1, 2, 3, 4, and 5;

g is selected from 0, 1, 2, 3, 4, and 5;

g' is selected from 0, 1, 2, 3, 4, and 5;

g" is selected from 0, 1, 2, 3, 4, and 5;

g"' is selected from 0, 1, 2, 3, 4, and 5;

s is selected from 0, 1, 2, 3, 4, and 5;

s' is selected from 0, 1, 2, 3, 4, and 5;

s" is selected from 0, 1, 2, 3, 4, and 5;

t is selected from 0, 1, 2, 3, 4, and 5;

t' is selected from 0, 1, 2, 3, 4, and 5;

and a pharmaceutically acceptable salt thereof.

42. A compound according to Claim 41, wherein the present invention provides a compound selected from the group:

1-(1,2-Dipalmitoyl-sn-glycero-3-phosphoethanolamino)-12-(cyclo(Arg-Gly-Asp-D-Phe-Lys))-dodecane-1,12-dione;

1-(1,2-Dipalmitoyl-sn-glycero-3-phosphoethanolamino)-12-(( $\omega$ -amino-PEG<sub>3400</sub>- $\alpha$ -carbonyl)-cyclo(Arg-Gly-Asp-D-Phe-Lys))-dodecane-1,12-dione; and,

1-(1,2-Dipalmitoyl-sn-glycero-3-phosphoethanolamino)-12-(( $\omega$ -amino-PEG<sub>3400</sub>- $\alpha$ -carbonyl)-Glu-(cyclo(Arg-Gly-Asp-D-Phe-Lys))<sub>2</sub>)-Dodecane-1,12-dione.

43. An ultrasound contrast agent composition, comprising:

(a) a compound of Claim 40, comprising: a cyclic pentapeptide that binds to the integrin  $\alpha_v\beta_3$ , a surfactant and a linking group between the cyclic pentapeptide and the surfactant;

(b) a parenterally acceptable carrier; and,  
(c) an echogenic gas.

44. An ultrasound contrast agent composition, further comprising: 1,2-dipalmitoyl-sn-glycero-3-phosphotidic acid, 1,2-dipalmitoyl-sn-glycero-3-phosphatidylcholine, and N-(methoxypolyethylene glycol 5000 carbamoyl)-1,2-dipalmitoyl-sn-glycero-3-phosphatidylethanolamine.

45. An ultrasound contrast agent composition, wherein, the echogenic gas is a C<sub>2-5</sub> perfluorocarbon.

46. A method of imaging cancer in a patient comprising: (1) administering, by injection or infusion, a ultrasound contrast agent composition of Claim 40 to a patient; and (2) imaging the patient using sonography.

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47. A method of imaging formation of new blood vessels in a patient comprising: (1) administering, by injection or infusion, a ultrasound contrast agent composition of Claim 5 40 to a patient; (2) imaging the area of the patient wherein the desired formation of new blood vessels is located.

48. A therapeutic radiopharmaceutical composition, 10 comprising:  
(a) a therapeutic radiopharmaceutical of Claim 11; and,  
(b) a parenterally acceptable carrier.

49. A diagnostic radiopharmaceutical composition, 15 comprising:  
(a) a diagnostic radiopharmaceutical, a MRI contrast agent, or a X-ray contrast agent of Claim 11; and,  
(b) a parenterally acceptable carrier. 20

50. A therapeutic radiopharmaceutical composition, comprising: a radiolabelled targeting moiety, wherein the targeting moiety is a compound Q of Claim 3 and the radiolabel 25 is a therapeutic isotope selected from the group:  $^{35}\text{S}$ ,  $^{32}\text{P}$ ,  $^{125}\text{I}$ ,  $^{131}\text{I}$ , and  $^{211}\text{At}$ .

51. A therapeutic radiopharmaceutical composition, 30 comprising: a radiolabelled targeting moiety, wherein the targeting moiety is a compound Q of Claim 5 and the radiolabel is a therapeutic isotope which is  $^{131}\text{I}$ .